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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/083,641	02/27/2002	Timothy A. Haystead	1579-647	1798

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EXAMINER	
GEBREYESUS, KAGNEW H	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 07/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/083,641	HAYSTEAD, TIMOTHY A.	
	Examiner	Art Unit	
	Kagnew H Gebreyesus	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *7-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) *1-22* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Details of

Election/Restrictions

I. Claims 1-16 are drawn to DNA, vectors, host cells and a processes of preparation, classified in class 536 subclass 23.2

II. Claims 17,18, are drawn to protein, classified in 435/196.

III. Claims 19, 21 and 22 are drawn to antibodies able to specifically bind to the myosin phosphatase targeting subunit kinase (MYPT) or portion thereof classified in class 530 subclass 387.9.

IV. Claim 20 is a method of screening for compounds that can modulate phosphorylation of MYPT1 by MYPT kinase classified in 453, subclass 15.

1. The nucleic acid sequences of group I and the polypeptides of group II comprise a chemically unrelated structure capable of separate manufacture, use and effect. The DNA comprises a nucleic acid sequence and the proteins of group II comprise amino acid sequences. The DNA has other utility besides encoding the proteins such as a hybridization probe, and the proteins can be made by other methods such as isolation from natural sources or chemical synthesis or *in-vitro* translation.

2. Inventions in Group II are related to group III by virtue of being the cognate antigen necessary for the production of the antibody. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the

product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case although the protein and the antibody are related, they are distinct inventions because they are physically and functionally distinct chemical entities and the protein product can be made by another and materially different process from the use for production of the antibody such as in a pharmaceutical composition on its own right.

3. Inventions in Group I and Group III are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the DNAs in Group I are separate and distinct from the antibodies in Group III as they are physically and functionally distinct chemical entities. Accordingly restriction is appropriate.

4. Inventions in Group I and Group IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the products in Group I are separate and distinct from the method of inventions in Group IV wherein the product in Group I can neither be made by or used in the method of screening described in the methods of Group IV. Accordingly restriction is appropriate.

5. Inventions Group II and IV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially

different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the proteins in Group II can be used to induce antibodies as in Group III for instance. Although the proteins in Group II are required in screening for a test compound, the proteins and the potential compound(s) in Group IV are physically and functionally distinct chemical entities.

6. Inventions in Group III and Group IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the method of Group IV neither make nor use the products in Group III.

7. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

8. The examiner has required restriction between product and process claims. During a telephone conversation with the attorney on 06/24/04 a provisional election was made with traverse to prosecute the invention of nucleic acids of claims 1-16. Affirmation of this election must be made by applicant in replying to this Office action. Claim 17-22 withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim

will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

9. In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112.

10. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35

U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claim 1-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The specification of the term "MYPT kinase" in claims 1-4 (from which claims 5-16 depend) is unclear and does not particularly point the term MYPT kinase by limiting the scope of the term to either a SEQ ID NO and/or to a protein having a specific functional characteristics. In claim 3 and 5 the inventor points to a nucleic acid sequence encoding an amino acid sequence in Fig. 9 which in turn is composed of 11 distinct sequences (SEQ ID NO: 7 to SEQ ID NO: 17), most of which are peptide sequences which are virtually certain to be devoid of any kinase activity. Therefor these claims are indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. For the purposes of further examination the term 'MYPT kinase" is assumed to include any protein which phosphorylates the MYPT sub-unit of smooth muscle protein phoshatase-1 (SMPP-1) at Thr^{697} but not at position Ser^{854}. Claims 3 and 5 are interpreted to include any MYPT

kinase encoding nucleic acid wherein the MYPT kinase comprises of any one of the peptide sequences of SEQ ID NO 7-17.

12. Claim 6 is indefinite in the recitation of "substantially identical" to SEQ ID NO 6. How many changes in SEQ ID NO 6 can be made and still be within the scope of the phrase "substantially identical".

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 1-7 and 9 –12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In these claims the scope of the nucleic acid sequence encoding MYPT kinase is not defined in full, clear and concise and exact terms such as to a SEQ ID NO and/or any protein specific functional characteristics. See the rejection under 112 second paragraph for the examiners interpretation of the scope of the claims.

14. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings above, or by disclosure of relevant, identifying

characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus (*See Eli Lilly,119 F.3d at 1568, 43 USPQ2d at 1406).*

15. A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The claims are drawn to isolated nucleic acids encoding MYPT kinase or mammalian MYPT kinase or fragments thereof with no indication of sequence and no description of the polypeptide encoded by the nucleic acids possessing a particular biological activity, nor any particular conserved structure or other disclosed distinguishing feature.

16. Thus, the claims are drawn to a genus of nucleic acids defined only by the name of the protein potentially encoded by the same. However, in the specification the nucleic acid sequence potentially encoding the MYPT was obtained from a rat aorta smooth muscle cDNA library that was screened with human ZIP kinase. To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, and methods of making the claimed product or any combination thereof. In the instant case, the only factor present is a

sequence referred to in fig. 8 with at least eight stop codons encoding the partial amino acid sequences of fig. 9 where eleven (11) different sequences are presented. As such this sequence clearly does not encode an MYPT kinase at all as it contains no open reading frame commensurate with the size of an MYPT kinase.

17. Furthermore isoformic variations of mammalian MYPT (the substrate for this enzyme) have been described (Fujioka M et al. Genomics 1998 Apr 1:49(1): 59-68) suggesting that there may be more than one isoform of the enzyme as well even within a single mammalian species which clearly indicates that the MYPT kinase of distinct mammals is likely to be distinct as well. No representative species of nucleic acid encoding other MYPT kinases is presented. Therefore the invention lacks provision to the scope of the claims. *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states that " applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the *invention*. The invention is, for purposes of the 'written description' *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of MYPT kinases encoded by the nucleic acids, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation.

18. Adequate written description requires more than presenting a nucleotide sequence as an invention but should show an open reading frame (ORF) that could be

transcribed and translated to a protein that in turn imparts the function and a description of the relationship between structure and function for the gene claimed.

19. Claims 1-7 and 9-12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

20. Claims 1, 7 and 9-12 are so broad as to encompass any nucleic acid encoding a protein capable of phosphorylating Thr^{697} of the MYPT subunit of smooth muscle cell PP-1. Claims 4-7 and 13-16 are even broader further including any fragment of at least 15 nucleotides of such nucleic acids. Claim 3 is so broad as to encompass any nucleic acid encoding a protein capable of phosphorylating Thr^{697} of the MYPT subunit of smooth muscle cell PP-1 which comprises any of the short peptide sequences of SEQ ID NOS: 7-17. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of nucleic acids encoding MYPT kinases or fragments thereof broadly encompassed by the claims.

21. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function.

22. However, in this case the disclosure is limited to the isolation of a single MYPT kinase protein and the disclosure of a nucleic acid sequence (i.e., that of Figure 8) that is clearly incorrect and incapable of encoding such a kinase or even likely being a fragment of a larger nucleic acid encoding such a protein as it includes no large open reading frame and includes many stop codons such that it cannot be a partial sequence.

23. While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions. The specification does not support the broad scope of the claims which encompass all nucleic acids encoding MYPT kinases or fragments thereof because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting MYPT kinase activity; (B) the general tolerance of MYPT kinases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably

correlated with the scope of the claims broadly including nucleic acids encoding MYPT kinases or fragments thereof. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of nucleic acids having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

24. Claim 1- 7 and 9 -16 are rejected under 35 U.S.C. 102(a) as being anticipated by Maki Murata-Hori et. al. FEBS Letter (1999) Vol. 451, 81-84 and Kawai T. et. al., Molecular and Cellular Biology, (1998) 18, no.3 1642-1651. Maki Murata-Hori et. al. disclose a nucleic acid encoding human ZIP kinase and the recombinant expression of the encoded kinase. The ZIP kinase encoded thereby comprises the sequence of SEQ ID NO 9. The nucleotide sequence of the HeLa ZIP kinase appears in the DDBJ/EMBL/GenBank database with the accession number AB022341. The nucleotide sequence for Kawai T. et. al., appears in the DDBJ/EMBL/GenBank database with the accession number AB007144 for the human and AB007143 for mouse.

25. The specification of the present application teaches that, the N-terminal region of the protein encoded by the 5' end of the human ZIPK (nucleotide sequence 19-930 bps)

exhibits the same functional characteristics as the "ZIP-like kinase" (MYPT kinase) encoded by the claimed nucleotide sequence(s). As such the full-length protein encoded by the nucleic acid of Maki Murata-Hori et. al inherently has these functional characteristics also and this anticipates the instant claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kagnew H Gebreyesus whose telephone number is 571-272-2937. The examiner can normally be reached on 8:30am-5:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Achutamurthy Ponnathapura can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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